

A Design of Experiments (DoE) Approach to Material Properties Optimization of Electrospun Nanofibers

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ABSTRACT: Using an electrospinning technique, polymer materials have been spun using electrostatic potential to create a fiber mat. To develop the electrospinning opportunities available for practical applications, it is important that a full understanding of process parameters is achieved. These fundamental principles will form the initial framework of future research with the effects on polymer output examined as the primary focus of this article. Poly(vinyl alcohol) (PVOH) and polylactic acid (PLA) polymer solutions were developed and a Design of Experiments (DoE) approach implemented, to determine whether the variation of factors led to significant effects on fiber output. Parameters altered were conductivity, concentration (% w/w), electrostatic potential, and the collection

distance at which the fiber was obtained. Results taken considered the fiber diameter, deposition rate of material, current achieved at the point of collection and whether or not the material was actually able to electrospin and visibly produce polymer fiber. The results of this work indicate the presence of interactions between the processing parameters and as such allow a fine tuning process to be used to adapt production of the micro- and nanofibers to suit a desired application with specific materials properties. © 2010 Wiley Periodicals, Inc. *J Appl Polym Sci* 117: 2251–2257, 2010

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INTRODUCTION

Electrospinning is a process for the development of polymer nanofibers using electrostatic potential to create a continuous fiber that can be collected in the form of a mat. Whilst the process of electrospinning itself was originally patented by Cooley,¹ Morton² and then subsequently by Formhals,³ it is only recently that it has gained significant momentum and worldwide recognition for its potential.⁴

Electrospinning can be applied using either a polymer solution, or in some instances as a melt.^{2,4} Whatever the polymer employed, there are many factors and variables that can affect the type and quantity of fiber that is produced. These variables can be identified in three broad categories, some of which have been listed previously.^{5,6} The first two are solution and process parameters with the final group being the environmental properties of the surrounding area (Table I).

In essence, this is a simple process to implement. Whilst there has been a great deal of work completed regarding the development of electrospinning of specific polymers, there is continued discussion regarding the effects of the individual processing conditions on the final electrospun fiber product.⁷ In order to optimize the process and generate fibers with desired properties, this paper focuses on the experimental analysis of how varying two or more experimental parameters effects the deposited nanofibers.

A wide range of polymers have been attempted to generate nanofibers from an electrospinning process.^{7,8} For our studies, it was decided to examine poly(vinyl alcohol) (PVOH) and polylactic acid (PLA). These two were chosen due to a combination of the volume of literature currently available, as well as their potential end-use applications. Various alterations to the collection parameters of PVOH including varying the molecular weight of the polymer⁹ or changing the conductivity^{10,11} and the pH of the solution¹² have been previously investigated. However, the literature is somewhat inconsistent in the conclusions, as well as failing to address how the combination of variables affects the final product.

Electrospinning is an inherently complex process with regard to physical parameters, as such, isolating

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TABLE I
Parameters Affecting the Electrospinning Process

Solution parameters	Process parameters	Environmental properties
Concentration	Electrostatic Potential	Temperature
Viscosity	Electric Field Strength	Humidity
Surface Tension	Electrostatic Field Shape	Local Atmosphere
Conductivity	Working Distance	Flow
Dielectric Constant	Feed Rate	Atmospheric Composition
Solvent Volatility	Orifice Diameter	Pressure

one collection parameter has limited relevance, in particular when trying to optimize properties for suitable applications. A recent theoretical paper discussed many of the collection parameters for electrospinning¹³ and determined that the most important parameters involved in the process were distance, charge density, jet radius, relaxation time, and viscosity. This article referred to previous experimental work in drawing conclusions but stated the data available to validate their model was lacking.

A useful tool in assessment of multiple factors is statistical analysis. Design of Experiments (DoE) methods which include response surface methodology (RSM) have been infrequently utilized for the electrospinning process. RSM was applied to electrospinning of polyacrylonitrile (PAN), the precursor to carbon fiber, and demonstrated that solution concentration played an important role in fiber diameter and distribution but applied voltage had little effect.¹⁴ Another study examining PAN found solution concentration, voltage and collector distance to be statistically significant in production of nanoscale fibers.¹⁵ A five level, five variable RSM study on electrospun PMMA investigated fiber diameter with respect to polymer concentration, distance, temperature, flow rate, and voltage. All variables were found to effect fiber diameter and there were no interaction effects.¹⁶ Earlier work on polystyrene did not use DoE but found four variables: solution concentration, voltage, distance, and flow rate to affect fiber diameter.¹⁷ DoE methods have also been applied to natural polymers specifically silk. The effect of spinning parameters, such as solution concentration, voltage, distance, and spinning rate on fiber diameter were determined. In one study the width of ribbons varied from 25 nm to 1800 nm¹⁸ and another successfully applied a second order polynomial to predict fiber diameter.¹⁹

Some of the more interesting applications for electrospun nanofibers include drug delivery²⁰ and tissue engineering of blood vessels and skin.²⁰ The high solubility of PVOH fibers in water limits the

usefulness of these fibers in such applications, although this does not completely rule them out altogether. One such polymer that is not water-soluble, and also has the advantage of being biodegradable is PLA, which has also previously been successfully electrospun.^{21,22}

PLA has been widely exploited for use in medical applications because of its excellent biocompatibility,²³ particularly in biocomposite scaffold structures containing hydroxyapatite²⁴ and copolymers or blends with poly(glycolic acid).²³ Although, much like PVOH, the process of electrospinning PLA has not been extensively characterized. Our aim was to characterize, using a statistical design of experiments (DoE) approach, how combinations of collection parameters affected the output of electrospun micro- and nano-fibers to optimize the process.

EXPERIMENTAL DETAILS

Electrospinning

PVOH ($M_w = 118,000 \text{ g mol}^{-1}$, degree of hydrolysis = 85–90%) was dissolved in distilled water at 60°C for 3 h with constant stirring (500 rpm). PLA was dissolved in CHCl_3 at 70°C overnight with constant stirring. The final concentration (% w/w) of both solutions was measured by removing the volatiles from a representative sample of the solutions on a rotary evaporator until constant mass was achieved. Samples of fiber mats were collected using an Electrospinz electrospinning machine.²⁵ The polymer solutions were passed through a polyethylene pipette tip, with a movable header tank controlling the rate of delivery. Varying distances (5–15 cm) and potential differences were used (5–15 kV) depending on the experimental design and samples were collected on a 10 × 10 cm aluminum plate.

Scanning electron microscopy (SEM)

Small samples of fiber mats were analysed with a SEM to determine the fiber diameter distribution. The fibers were gold sputter coated and the mats were imaged using a Zeiss Sigma microscope. For each sample, 8–10 nonoverlapping images were taken and using Image Tool,²⁶ the diameter of the each clearly visible fiber was measured. The length-weighted average fiber diameter was then calculated using the data collected from each image.

RESULTS AND DISCUSSION

Initial DoE Table

As previously discussed, there are many factors that can influence electrospinning. Initially, two of the process parameters (electrostatic potential and collection

TABLE II
DoE Matrix for Electrospinning

Run	Conductivity	Conc. (% w/w)	Potential (kV)	Collection distance (cm)
1	No Salt	Low	High	Low
2	Salt	High	Low	Low
3	No Salt	High	High	High
4	No Salt	Medium	Medium	Medium
5	No Salt	Low	Low	High
6	Salt	Low	High	Low
7	Salt	Medium	Medium	Medium
8	Salt	High	High	High
9	No Salt	Medium	Medium	Medium
10	No Salt	High	Low	Low
11	Salt	Low	Low	High

distance) and two of the solution parameters (concentration and dielectric constant) were varied. These factors were chosen as it was believed that they have the combination of being the simplest to control but also have the greatest influence on the electrospinning process. A matrix was constructed to test the variations in two of the process parameters of the electrospinning process (electrostatic potential and collection distance) and two of the solution parameters (concentration and conductivity) (Table II).

The addition of a small amount of potassium chloride (KCl) to an aqueous solution (1.0% w/w) will affect the dielectric constant, and therefore, the conductivity of the solution. Other material properties, such as the vapor pressure, are assumed to be unaffected given the small amount added. Given that the solution requires a high level of voltage applied to form the Taylor cone,²⁷ the ability of the solution to conduct electricity is paramount.

To determine how to optimize the parameters for any given situation, several outputs were measured. The flow rate was adjusted to ensure that the droplet at the end of the electrospinning apparatus remained of a constant size, i.e., did not oscillate.

We found that oscillations tended to form electro-sprayed material as opposed to electrospun fibers. Initially, whether the run produced a visible quantity of electrospun fiber was also recorded. The fiber was collected on a pre-weighed aluminum plate, which allowed the deposition rate to be collected, and the current was also measured during the process. The fibers were analyzed using SEM (Fig. 1) to observe the overall structure of the collected mats and the length-weighted average diameter of the fibers was determined using Image Tool.²⁶ Table III shows the results for PVOH in H₂O.

In all cases, the current was recorded at the start at the run and showed a small decrease (typically around 0.1 μ A) over the course of the 15 min experiment. This slight reduction is because of the formation of the layer of polymer effectively acting as an insulator. However, to minimize errors in the measurement of the deposition rate the shortest collection period (15 min) was used to ensure sensible data was recorded.

Runs 1 and 10 failed to produce fiber, whilst a gain in mass was observed on the collection plates, analysis by SEM showed no fiber was present.

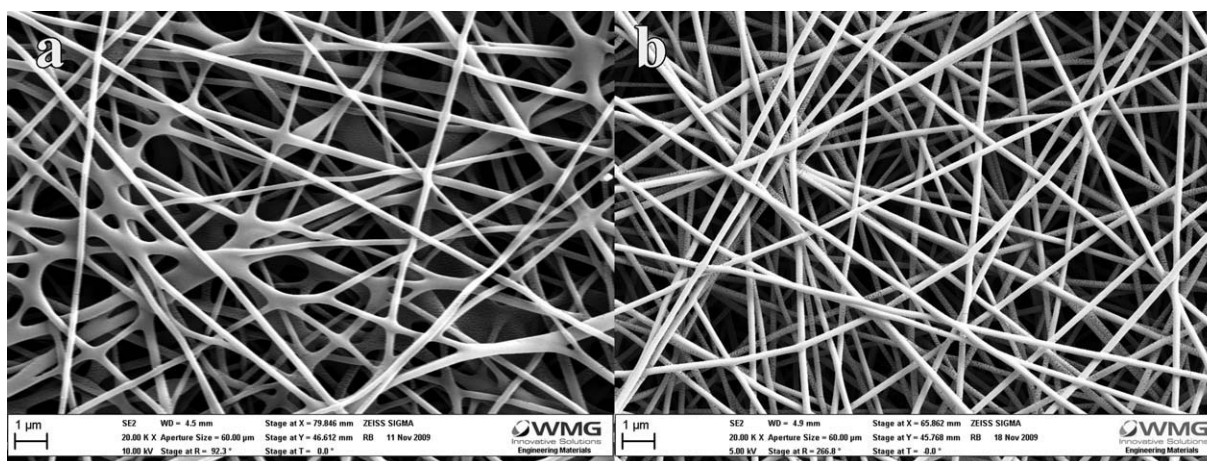


Figure 1 Example distribution of fiber diameters.

TABLE III
Experimental Results for Electrospinning of PVOH Fibers

Run	Salt Addition ^a	Concentration (% w/w)	Pot. (kV)	Distance (cm)	Fiber produced	Deposition rate (mg h ⁻¹)	Current (μA)	Fiber diameter (μm)
1	No Salt	6	15	5	No ^b	–	–	–
2	Salt	13.4	5	5	No	–	–	–
3	No Salt	13.4	15	15	Yes	13.6	2.71	0.73 ± 0.28
4	No Salt	10.6	10	10	Yes	63.2	1.45	0.55 ± 0.18
5	No Salt	6	5	15	No	–	–	–
6	Salt	6	15	5	Yes	46.8	13.9	0.26 ± 0.10
7	Salt	10.6	10	10	Yes	68.8	2.3	0.61 ± 0.20
8	Salt	13.4	15	15	No	–	–	–
9	No Salt	10.6	10	10	Yes	61.8	1.6	0.48 ± 0.13
10	No Salt	13.4	5	5	No ^b	–	–	–
11	Salt	6	5	15	No	–	–	–

^a Salt added was potassium chloride at a 1.0% w/w concentration.

^b Runs 1 and 10 both showed an increase in mass but SEM analysis showed no fibers present.

Instead, small droplets of PVOH were observed, characteristic of electrosprayed material.²⁸

Initial observations show that the addition of 1% potassium chloride (KCl) to the 13.6% w/w PVOH solution prevents successful electrospinning (runs 2 and 8). The addition of KCl increases the apparent viscosity of the PVOH solution by disrupting the inter and intra-chain hydrogen bonding between the polymer chains, also increasing the solubility of the polymers.²⁹ This increase in viscosity makes the droplet that is formed at the end of the tip too stable, and cannot be disrupted even when 15 kV is applied (run 8).

PVOH spins more slowly than PLA, with deposition rates only reaching 68.8 mg h⁻¹ (run 7). The best parameters for fast collection of PVOH fibers are when the median parameters are applied; in this case an electrostatic potential of 10 kV, a collection distance of 10 cm and a concentration of 10% w/w. The addition of KCl appears to have a negligible effect (run 4 vs. run 7).

The current varies with the collection distance and the applied voltage. The highest current recorded (run 6) is when the distance is short (i.e. reduced resistance) and the voltage is high. The lowest observed current (run 10) was when the voltage was low, although the distance was also short on that run. Runs that had low voltage and a long distance (runs 5 and 11) failed to produce fiber.

The solution with the highest concentration produces the fibers with the largest diameter (run 3). This is the result of more polymer being present in the Taylor cone when the fiber is generated. Similarly, the run with the lowest concentration (run 6) has the smallest fiber diameter. There were not enough successful runs to draw conclusions about the effect of collection distance or electrostatic potential on the fiber diameter, whilst the addition of salt has a negligible effect (runs 4, 7, and 9).

The results for PLA in CHCl₃ are summarized in Table IV. The only difference between the two sets of experiments is that only 0.1% w/w KCl was

TABLE IV
Experimental Results for Electrospinning of PLA Fibers

Run	Cond. ^a	Concentration (% w/w)	Pot. (kV)	Distance (cm)	Fiber produced	Dep. Rate (mg h ⁻¹)	Current (μA)	Fiber diameter (μm)
12	No Salt	5.0	15	5	Yes	105.6	0.28	2.28 ± 1.24
13	Salt	10.0	5	5	No	–	–	–
14	No Salt	10.0	15	15	Yes	7.6	0.25	– ^b
15	No Salt	7.5	10	10	Yes	31.6	0.09	1.70 ± 1.04
16	No Salt	5.0	5	15	Yes	58.4	0.01	5.29 ± 1.36
17	Salt	5.0	15	5	Yes	292.8	0.23	1.53 ± 1.02
18	Salt	7.5	10	10	Yes	31.6	0.08	2.94 ± 2.01
19	Salt	10.0	15	15	No	–	–	–
20	No Salt	7.5	10	10	Yes	41.0	0.09	1.63 ± 1.18
21	No Salt	10.0	5	5	No	–	–	–
22	Salt	5.0	5	15	Yes	67.2	0.01	2.26 ± 1.35

^a Salt added was potassium chloride at 0.0% w/w concentration.

^b Run 14 produced such a small amount of fiber that it was unable to be analysed under the SEM.

TABLE V
PVOH DoE Table II

Run	Concentration (% w/w)	Pot. (kV)	Distance (cm)	Deposition rate (mg h ⁻¹)	Fiber diameter (μm)
23	10.6	15	5	59.7	1.11 ± 0.67
24	6	10	10	21.5	0.23 ± 0.05
25	10.6	10	10	38.3	0.51 ± 0.13
26	10.6	10	5	50.8	1.31 ± 0.79
27	6.0	15	10	40.0	0.17 ± 0.04
28	6.0	10	5	59.2	0.24 ± 0.04
29	10.6	15	10	25.4	0.66 ± 0.23
30	6.0	15	5	62.7	0.24 ± 0.06

added because of the solubility in CHCl₃. PLA has a much narrower concentration range for the production of fiber. With PVOH it is possible to spin from 6% w/w¹⁰ up to our own observations of around 13.6% w/w. PLA has been shown to produce fibers at concentrations as low as 2.0%,²¹ and we were unable to produce fiber from concentrations greater than 7.5% w/w.

PLA spins at a faster rate than PVOH, with deposition rates observed up to 292.8 mg h⁻¹ (run 17). The number of successful runs increased from PVOH to PLA, indicating that PLA in CHCl₃ is an easier material to spin. However, PLA needs to be closely monitored, because of the high volatility of the solvent solid polymer is formed on the tip of the cone, obstructing and preventing further fiber being produced. This phenomenon has been recorded previously.^{30,31}

The deposition rate is faster when the voltage is high, but the concentration is low, with the 2 fastest runs (runs 12 and 17) both coming when the voltage was set at 15 kV and the concentration at 5.0% w/w. Lower concentrations and collection distances are beneficial for faster deposition rates of PLA. The observed current shows the same expected pattern as with the PVOH.

The fiber diameters do not show the same pattern as with PVOH. The runs with the lowest concentration (12, 16, and 22) show the largest diameters with run 16 in particular having an average fiber diameter twice as large as any of the other runs. At concentrations below 5% w/w for PLA, the pattern of low concentrations producing the thinnest fibers has previously been observed.³²

The addition of KCl affects the fiber diameter, increasing not only the average fiber diameter but also the range of diameters produced. There is a relationship between the runs with the fastest deposition rates and those with the smallest fiber diameters. We have postulated that the speed of deposition causes a thinning effect in the fibers. Certainly with polymer extrusion (or pultrusion) the quicker you draw a fiber the smaller it is.

Refining the experimental design

The large number of unsuccessful runs meant it was impossible to carry out a statistical analysis of this work. Also, the human error introduced by near-continuous clearing of polymer from the tip prevented sufficiently accurate results being recorded with PLA. Therefore, only the PVOH was investigated further. Based on the results from the previous DoE Tables, it was determined that the most important factors were concentration, potential difference, and collection distance. A full factorial design on two levels was implemented, and the results carried out in triplicate so as to comprehensively investigate the parameters. The responses of deposition rate and fiber diameter were again measured. The results are summarized in Table V.

To show whether or not average fiber diameter and the standard deviation is a valid output for the collected fibers, histograms were plotted to assess the distribution of fibers. In all cases, the distribution of fibers is unimodal, an example of which is shown in Figure 2. As such, standard deviation becomes a useful measure of how well controlled the electrospinning process is. A low deviation means that the distribution of fiber diameters is tighter, and therefore, the control over the process

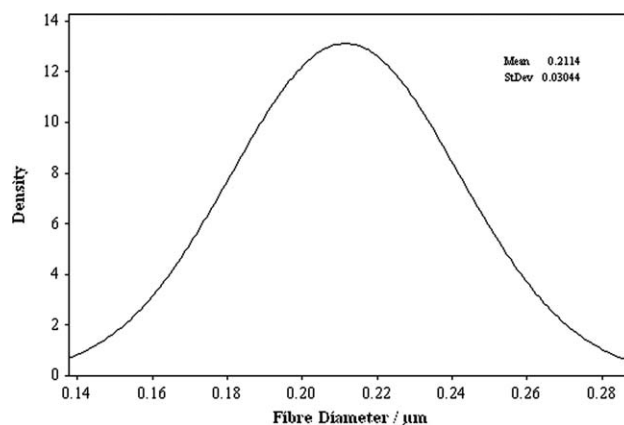


Figure 2 Example SEM images of electrospun PVOH nanofibers.

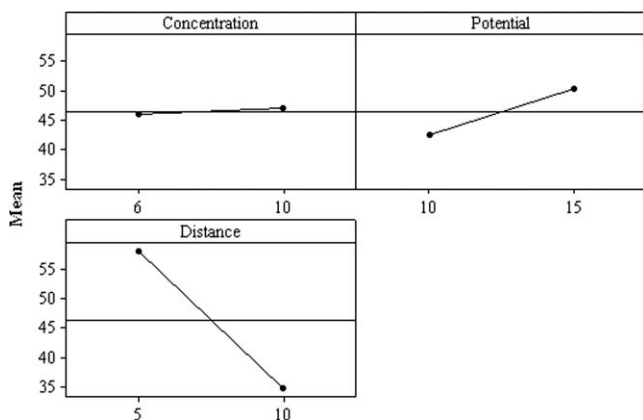


Figure 3 Main effects plot for deposition rate.

is greater. For example, run 24 demonstrates good control, with the standard deviation only 0.05 μm , whereas run 26 exhibits poor control with a deviation of 0.79 μm .

Again, the results show that there is considerable variance to both the deposition rate and the fiber diameter depending on how the fiber is collected. The results were processed to produce main effects plots and interaction plots to determine the effect of the factors and interaction between factors.

The values presented in Figure 3 are the means at each level under consideration for the deposition rate. Each small box has two means connected by a solid line. The steeper the gradient of the line, the larger the difference between the two means and therefore the greater the influence of the factor on the deposition rate. As a common factor in PVOH, and one that is to be expected, increasing the potential difference from 10 to 15 kV increases the deposition rate. The deposition rate shows a slight increase when the concentration is increased for PVOH from 6% to 10.6% w/w. Conversely, increasing the distance between the collection point and the tip slows down the rate of deposition, possibly due to a reduction in the force attracting the fiber across to the plate.

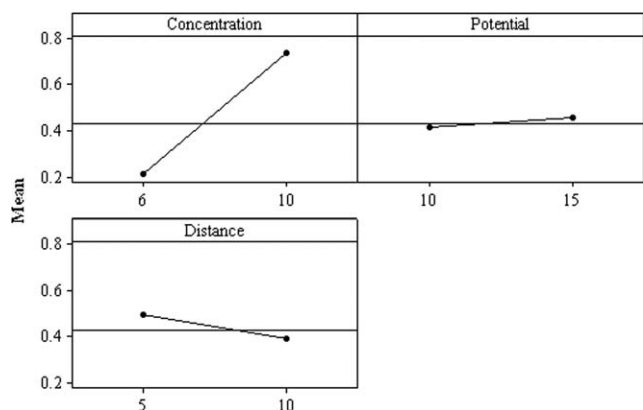


Figure 4 Main effects plot for fiber diameter.

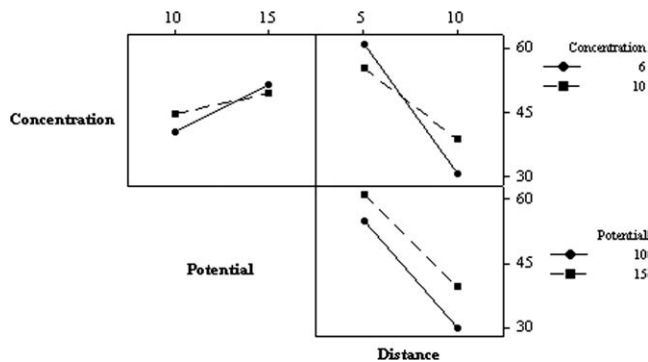


Figure 5 Interactions plot for deposition rate.

Similar main effects plots were drawn for the changes in the average fiber diameter for PVOH (Fig. 4). An increase in concentration caused an increase in fiber diameter. As the solutions are more concentrated, there is more polymer available to be spun at the point where the droplet breaks down. Thus, a thicker fiber is produced from the droplet in a jet toward the counter electrode. This is certainly in agreement provided in the theoretical model discussed by Thompson et al.¹³ An increase in the distance at which the fibers are collected caused a slight decrease in the average fiber diameter for both types of polymer. This is perhaps intuitive; drawing an analogy to a standard pultrusion process, you would expect the fibers to be thinner the further they were pulled out, assuming the speed remains constant. The theoretical model considers the difference in morphology of changing the collection distance but not the average fiber diameter, comparing it only to Nylon-6.^{13,33} Increasing the potential increases the fiber diameter for PVOH, although the change in average diameter across 10 to 15 kV is minimal, as shown by the relatively flat line.

Considering the interactions plot for deposition rate when using PVOH (Fig. 5) and fiber diameter (Fig. 6) gives indicators as to how the factors affect the output parameters in combination with each other. Indication is given by the relative slopes of

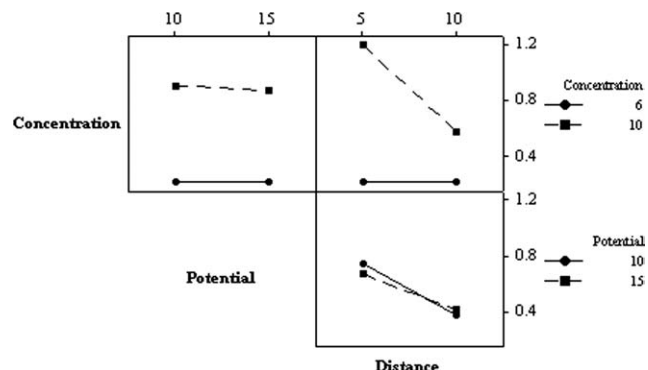


Figure 6 Interactions plot for fiber diameter.

the two lines on each individual box. For example, with respect to fiber diameter there is no interaction between concentration and potential because the two lines have identical gradients (Fig. 6). This is likely because concentration is a defining factor for fiber diameter and has a significantly greater influence than the potential difference.

On the same figure, there is no interaction between electrostatic potential and distance. In general, there are limited interactions of no statistical significance between concentration and collection distance with respect to both fiber diameter and deposition rate. These findings are to be expected; the presence of interactions between factors in such a complex process as electrospinning has been assumed, but these results go some of the way to proving their existence.

CONCLUSIONS

Whilst electrospinning is based upon numerous physical phenomena, it is still unclear as to the extent of the interactions between them. Statistical analysis has shown the likelihood of interactions between the collection parameters, and it is clear that the process can be readily adapted to produce fibers of a wide range of diameters (0.16 to 5.29 μm) with varying rates of deposition (7.6–298.0 mg h^{-1}) depending on the choice of polymer and the parameters used to collect the fibers.

PLA produces fibers that are generally bigger than the nanofibrous PVOH structures that are generated, although PLA produces those mats at a much faster rate. PVOH was also shown to be much easier to control, producing fibers with much narrower ranges of diameter distribution. The level of control was also hindered by solvent evaporation causing the PLA to crystallize on the tip. PVOH also shows a greater range of spinnable concentrations, although the number of parameters which successfully produce fibers is smaller than when PLA is applied.

Statistical analysis of this DoE approach has indicated that the collection parameters have interactions causing changes in the output of the fiber and the subsequent materials properties. These interactions can be used to tune the production of micro- or nanofibers to (in this instance) a desired fiber diameter or deposition rate.

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